Biomedical Update:

Epstein-Barr infection, mental problems linked

In recent years, scientists have tentatively linked several infectious agents to psychiatric symptoms. New research suggests that Epstein-Barr, the common virus that causes mononucleosis, should be added to this list.

June Caruso and colleagues identified five children who developed cognitive and neurological problems after contracting Epstein-Barr. Their symptoms included seizures, obsessive-compulsive behavior, cognitive deterioration, loss of speech and language skills, impulsiveness, and inappropriate behavior. Magnetic resonance imaging (MRI) scans of the children revealed abnormalities in all cases.

The researchers say that individuals who develop Epstein-Barr encephalitis may not present with typical symptoms of mononucleosis, and that serum tests may be negative. They recommend that patients who present with sudden symptoms of perseveration, impulsivity, seizures, abnormal emotional changes, and obsessive-compulsive behavior be evaluated for Epstein-Barr infection.

In earlier research, investigators linked strep infections to a disorder they have named pediatric autoimmune neurological disorders, or PANDAS. In addition to causing hyperactivity, tics, and obsessive compulsive behaviors, PANDAS has been associated with some cases of autism (see ARRI 13/1). Borna virus, also being investigated as a possible cause of autism, is associated with depression (see ARRI 10/3).

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"Persistent preceding focal neurologic deficits in children with chronic Epstein-Barr virus encephalitis," J. M. Caruso, G. A. Tung, G. G. Gascon, J. Rogg, L. Davis, and W. D. Brown, *Journal of Child Neurology*, Vol. 15, No. 12, December 2000, pp. 791-796. Address: J. M. Caruso, Department of Pediatric Neurology, Children's National Medical Center, Washington, D.C. 20010.

PMS therapy beneficial

Research indicates that females with autism experience significantly worse aggression and self-injury immediately before their monthly periods—possibly due to premenstrual syndrome (PMS). A recent study in the *British Medical Journal* suggests that in the general population, these symptoms can be eased by a readily available herbal remedy.

Rudiger Schellenberg studied 170 women with PMS, assigning them randomly to receive either a daily supplement containing 20 mg of *agnus castus*, an extract of the fruit of the chaste tree, or a placebo. Schellenberg evaluated the women's PMS symptoms at baseline, and after three monthly cycles, and reports that the herbal supplement was superior in relieving irritability, headache, mood swings, and breast tenderness, with more than half of the treatment group showing greater than 50 percent improvement in symptoms, compared to only a quarter of those taking the placebo. No significant side effects were seen.

Schellenberg concludes, "Dry extract of *agnus castus* fruit is an effective and well tolerated treatment for the relief of symptoms of the premenstrual syndrome."

In earlier research (see ARRI 14/3), E. H. Quint and colleagues found that 18 percent of developmentally disabled females experienced cyclic behavioral worsening due to PMS or menstrual pain. In that study, the researchers found that nonsteroidal anti-inflammatory drugs (NSAIDs) reduced behavior problems.

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"Treatment for the premenstrual syndrome with agnus castus fruit extract: prospective, randomised, placebo controlled study," Rudiger Schellenberg, *British Medical Journal*, Vol. 322, 2001, pp. 134-137. Address: Rudiger Schellenberg, Institute for Health Care and Science, 35625 Hüttenberg, Germany, rued.schellenberg.med@t-online.de.

Olanzapine somewhat effective against SIB

The psychotropic drug olanzapine (Zyprexa) may reduce self-injurious behavior (SIB) in some individuals with developmental disabilities, according to a recent study by M. McDonough and colleagues.

The researchers administered olanzapine, in dosages ranging from 5 to 15 mg, to seven mentally retarded patients with stereotyped SIB. (Existing medications were continued as well.) The study included a six-week baseline period and 15 weeks of treatment.

McDonough et al. report, "Out of the seven subjects, three showed a clear improvement, one showed a marginal improvement, one deteriorated, and the data [were] equivocal for the remaining two individuals."

The only adverse effect seen in study subjects was transient sleepiness. Side effects reported in other studies include decreased alertness, anxiety, nervousness, agitation, constipation, dry mouth, and dizziness.

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"Olanzapine for chronic, stereotypic self-injurious behaviour: a pilot study in seven adults with intellectual disability," M. McDonough, J. Hillery, and N. Kennedy, *Journal of Intellectual Disability Research*, Vol. 44, Part 6, December 2000, pp. 677-684. Address: M. McDonough, Behavioral Psychotherapy Unit, Maudsley Hospital, Denmark Hill, London, U.K.

Oxytocin-deprived mice lack social memory

Mice genetically engineered to lack the gene for the hormone oxytocin appear to have severe deficits in "social memory," according to recent research by J. N. Ferguson and colleagues. The findings parallel research linking oxytocin abnormalities to autism.

Ferguson et al. placed female mice in the cages of normal or oxytocin-deficient male mice. The normal male mice sniffed "stranger" mice carefully on the first visit, but sniffed them less thoroughly as they became familiar with the female mice through repeated contact. The mice lacking oxytocin, however, sniffed each female mouse thoroughly at each visit, as though the female were a stranger. However, the oxytocin-lacking mice had no difficulty running mazes, showing that their spatial memory was intact. Additional tests revealed that their sense of smell was normal as well.

The researchers also report that when they administered oxytocin to the mice lacking the hormone, the hormone restored the animals' social memory. Conversely, normal mice given a drug that blocks oxytocin's effects developed "a social amnesia-like effect."

The researchers conclude, "Our data indicate that oxytocin is necessary for the normal development of social memory in mice and support the hypothesis that social memory has a neural basis distinct from other forms of memory."

Several lines of research link oxytocin abnormalities to autism. Eric Hollander has reported that 60 percent of autistic children in his clinic were exposed to pitocin (an artificial form of oxytocin used to induce labor) at birth, while only 20 percent of control children were exposed (see ARRI 11/4). Conversely, supplemental oxytocin may improve symptoms of autism; Hollander et al. have found that some autistic subjects infused with oxytocin became more verbal, energetic, happy, and less anxious during treatment.

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"Social amnesia in mice lacking the oxytocin gene," J. N. Ferguson, L. J. Young, E. F. Hearn, M. M. Matzuk, T. R. Insel, and J. T. Winslow. *Nature Genetics*, Vol. 25, No. 3, July 2000, pp. 284-288. Address: J. N. Ferguson, Center for Behavioral Neuroscience, Emory University School of Medicine, Atlanta, GA.

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